

**SUBSTITUTE SHEET (RULE 26)** 

WO 97/46679 PCT/US97/09709

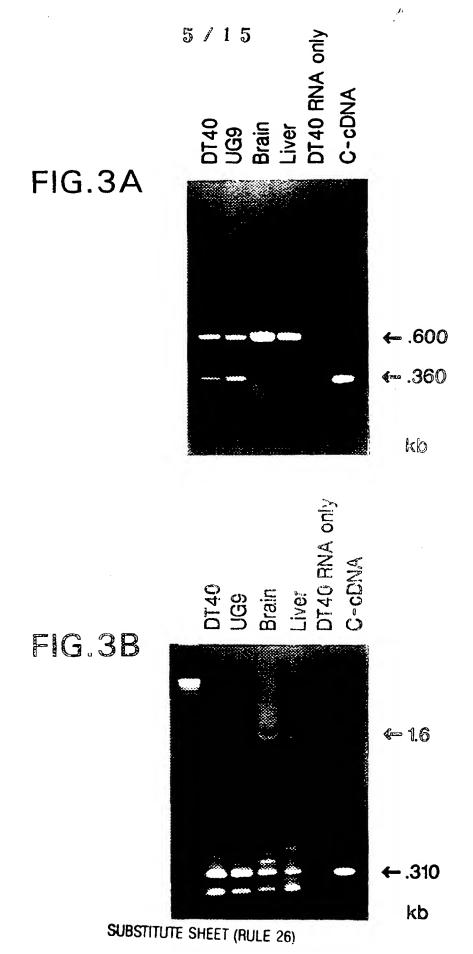


FIG.4A

← CmRNA-2 (~1.7 kb)

FIG.4B

Cyclin C

F16.40

- \* <- B2 (-1.6 kb)

FIG.4D

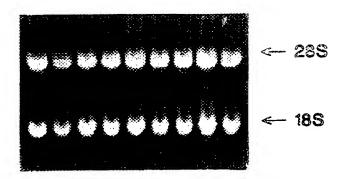


FIG.4E

%G1 **%**S

10 12 14 0 34 33 20 46 13 27 33 36 61 43 38 60 10 43 73 32 %G2/M 62 44 23

Cyclin C Truncated Cyclin C

FIG.5A

43 -

29 –

19 -

16.5 -

kDa

VIII DT40 DT40

FIG.5B

Cyclin C -

Truncated Cyclin C - (19 kDa)

+ Competition

1	MVAPRPERRVVEFYQGKLCSMAGNFWQSSHYLQW1LDRQD
41	LLKERQKDLKFLSEEEYWKLQIFFTNVIQALGEHLKLRQQ
81	VIATATVYFKRFYARYSLKSIDPVLMAPTCVFLASKVEEF
121	GVVSNTRLIAAATSVLKTRFSYAFPKEFPYRMNHILECEF
161	YLLELMDCCLIVYHPYRPLLQYVQDMGQEDMLLPLAWRIV
201	NDTYRTDLCLLYPPFMIALACLHVACVVQQKDARQWFAEL
241	SVDMEKILEIIRVILKLYEQWKNFDERKEMATILSKMPKP
281	KPPPNSEGEQGPNGSQNSSYSQS///////////////////////////////
321	//// FRRIP

FIG.6

9 / 1 5

## FIG.74

4	yaycycyyttaccyyacygygctygygtctatyytcyctccycycyctcc 
21	gccgcgtggtgctttttatcagggcaagctgtgttccatggcagggaac
101	ttttggcagagctcccactatttgcaatggattttggataaacaagatct
151	gttgaaggagcgccaaaaggatttaaagtttctctcagaggaagaatatt
201	ggaagttacaaatattttttacaaatgttatccaagcattaggtgaacat
251	cttaaattaagacaacaagttattgccactgctacggtatatttcaagag
301	attctatgccaggtattctctgaaaagtatagatcctgtattaatggctc

351	ctacatgtgtgttttttggcatccaaagtagaggaatttggagtagtttca
401	aatacaagattgattgctgctgctacttctgtattaaaaactagattttc
451	atatgcctttccaaaggaatttccttataggatgaatcatatattagaat
501	gtgaattctatctgttagaactaatggattgttgcttgatagtgtatcat
551	ccttatagacctttgctccagtatgtgcaggacatgggccaagaagacat
601	gttgcttccccttgcatggaggatagtgaatgatacctacagaacggatc
651	tttgcctactgtatcctcctttcatgatagctttagcttgcctacatgta

# FIG.7C

701	gcctgtgttgtacagcagaaagatgccaggcaatggtttgctgagctttc
751	tgtggatatggaaaagattttggaaataatcagggttattttaaaactat
801	atgagcagtggaagaatttcgatgagagaaaagagatggcaaccattctt
851	agtaagatgccaaaaccaaaccacctccaaaca//////////
901	//////////////////////////////////////
951	tggaagtcagaactctagctacagccaatcttaaaaacattccgaagaatt
1001	ccatag

Ţ	MVAPRPLRRVVLFYQGKLCSMAGNFWQSSHYLQWILDKQL
41	LLKERQKDLKFLSEEEYWKLQIFFTNVIQALGEHLKLRQQ
81	VIATATVYFKRFYARYSLKSIDPVLMAPTCVFLASKVEEF
121	GVVSNTRLIAAATSVLKTRFSYAFPKEFPYRMNHILECEF
161	YLLELM////////DCCLIVYHPYRPLLQYVQDMGVSKSSVINRLKHF*
201	QEDMLLPLAWRIVNDTYRTDLCLLYPPFMIALACLHVACV
241	VQQKDARQWFAELSVDMEKILEIIRVILKLYEQWKNFDEF
281	KEMATILSKMPKPKPPPNSEGEOGPNGSONSSYSOS

FIG.8

1	<pre>gagcgcggttaccggacggctgggtctatggtcgctccgcggccgctcc</pre>
51	gccgcgtggtgcttttttatcagggcaagctgtgttccatggcagggaac
101	ttttggcagagctcccactatttgcaatggattttggataaacaagatct
151	gttgaaggagcgccaaaaggatttaaagtttctctcagaggaagaatatt
201	ggaagttacaaatattttttacaaatgttatccaagcattaggtgaacat
251	cttaaattaagacaacaagttattgccactgctacggtatatttcaagag
301	attctatgccaggtattctctgaaaagtatagatcctgtattaatggctc
351	ctacatgtgtgtttttggcatccaaagtagaggaatttggagtagtttca
401	aatacaagattgattgctgctgctacttctgtattaaaaactagattttc
451	atatgcctttccaaaggaatttccttataggatgaatcatatattagaat
501	Exon 7 gtgaattctatctgttagaactaatg//////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////

FIG.9A

	14/15 //////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//// :::::::: gata :::::::
527	Exon 8 gattgttgcttgatagtgtatcatccttatagacctttgctccagtatgtg
	caggacatgggccaagaagacatgttgcttccccttgcat::::::::::
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////
	//////////////////////////////////////

FIG.9B

Exon 9
ggaggatagtgaatgatacctacagaacggatc

622 tttgcctactgtatcctcctttcatgatagctttagcttgcctacatgta

673 gcctgtgttgtacagcagaaagatgccaggcaatggtttgctgagctttc

724 tgtggatatggaaaagattttggaaataatcagggttattttaaaactat

775 atgagcagtggaagaatttcgatgagagaaaagagtggcaaccattctt

826 agtaagatgccaaaaccaaaaccacctccaaacagtcaaggaggg

877 tccaaataaggcaataatctattgcaaagttacttggaagtcagaactct

928 agctacagccaatcttaa

## FIG.9C

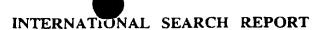
## INTERNATIONAL SEARCH REPORT

nal Application No PCT/US 97/09709

A. CLASSIFICATION OF SUBJECT MATTER
1PC 6 C12N15/12 C07K14/465 CO7K14/47 C07K16/18 C12N5/10 A01K67/027 A61K38/17 A61K31/70 A61K48/00 C1201/68 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12N C07K A01K A61K C12Q IPC 6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Category ' Relevant to claim No. X EMBL Database entry GG40873; 22,23 Accession number U40873: 20.11.1995; Li H. et al.: 'Gallus gallus cyclin C mRNA.' XP002039161 see abstract Α CELL, 1 - 32vol. 66, 1991, pages 1197-1206, XP002039130 LEW D.J. ET AL.: "Isolation of three novel human cyclins by rescue of G1 cyclin (Cln) function in yeast. cited in the application see the whole document, especially Fig. 3A and from page 1199, right column, last paragraph to page 1200, right column, bottom line -/--Further documents are listed in the continuation of box C. Ix∃ Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document referring to an oral disclosure, use, exhibition or document is combined with one or more other such docu-ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 1 6. 03. 97 2 September 1997 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Mandl, B Fax: (+31-70) 340-3016

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r. Ial Application No PCT/US 97/09709

		PC1/US 97/09/09
C.(Conunu	agon) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 666 270 A (BRISTOL-MYERS SQUIBB COMPANY) 9 August 1995 see the whole document, especially page 4, lines 46-58 and page 7, lines 44-57	1-32
Α	WO 93 24514 A (MITOTIX) 9 December 1993 see the whole document, especially page from 6, line 27 to page 7, line 14 and from page 20, line 16 to page 21, line 11	1-32
A	PROC. NATL. ACAD. SCI. USA, vol. 92, 1995, pages 8871-8875, XP002039131 TASSAN JP. ET AL.: "Identification of human cyclin-dependent kinase 8, a putative protein kinase partner for cyclin C." cited in the application	1-32
A	SCIENCE, vol. 240, 1988, pages 1544-1546, XP002039132 JASKULSKI D. ET AL.: "Inhibition of cellular proliferation by antisense oligodeoxynucleotides to PCNA cyclin." see the whole document	21,27
P,X	ONCOGENE, vol. 13, no. 4, 15 August 1996, pages 705-712, XP002039133 LI H. ET AL.: "Alternatively spliced cyclin C mRNA is widely expressed, cell cycle regulated, and encodes a truncated cyclin box." see the whole document	1-32

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Please see Further Information sheet enclosed.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

#### INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 97/ 09709

FURTHER INFORMATION CONTINUED FROM	PCT/ISA/210
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Remark: Although claim 27 and claims 28-30 partially, as far as they concern an in vivo method, are directed to a method of treatment of (diagnostic method practised on) the human/animal body the search has been carried out and based on the alleged effects of the compound/composition.

#### INTERNATIONAL SEARCH REPORT

on on patent family members

nal Application No PCT/US 97/09709

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0666270 A	09-08-95	US 5625031 A CA 2140379 A JP 7316196 A	29-04-97 09-08-95 05-12-95
WO 9324514 A	09-12-93	NONE	

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